Los Angeles Times

Business; Business Desk
In its Lap-Band decision, FDA takes light approach

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1,125 words
23 February 2011
Los Angeles Times
LATM
Home Edition
B-1
English

In 1960, a young inspector for the Food and Drug Administration faced down a powerful drug company by rejecting its application to sell a morning-sickness drug in the United States.

The company, Richardson-Merrell, griped about her repeated demands for more safety data. They complained to her superiors, branding her as a nitpicker. But she stood firm.

The drug in question was thalidomide, and worldwide as many as 12,000 children were born with severe birth defects after their mothers used it. In the U.S., where Frances Oldham Kelsey blocked Merrell from distributing the drug except to a few doctors for "experimental" trials, the toll was 17. Thanks to her, the FDA gained a reputation as a vigilant watchdog.

Today's FDA isn't that FDA.

Today's FDA just approved an application by the drug company Allergan to expand the target market of its **L a p - B a n d** weight-loss device potentially by tens of millions of patients. How much safety data did the FDA review before giving Allergan the green light? Mainly the results of one year of study of 149 patients, and partial data from a second year. Today's FDA evidently can be steamrollered.

Kelsey has said that she demanded more information from Merrell, thalidomide's U.S. manufacturer, because its history of conflicts with the agency made her suspicious. Is there any reason to mistrust Allergan? Let's look at the record.

In September, Allergan pleaded guilty to one criminal count and paid $600 million in fines and penalties to settle federal charges that it had illegally marketed its marquee product, Botox, for uses the FDA hadn't approved. The guilty plea was for "misbranding" Botox, a misdemeanor.

In accepting the plea bargain, the government charged that the company had made under-the-table payments to doctors who used Botox to treat unapproved conditions, created front groups and websites to push the broader uses of the drug while concealing Allergan's backing, and coached physicians to over-diagnose a condition for which Botox could be legally marketed so it could sell more product. Allergan says for the record that it doesn't believe there is merit to those allegations "factually or legally."

Allergan took these steps, the government contended, because the approved uses had meager sales potential. The most prevalent condition for which Botox treatment was approved, cervical dystonia, is a painful neck spasm that affects only about 27,000 people in the U.S. Allergan wanted doctors to prescribe Botox for headaches -- not an approved use, but a potentially huge market -- so it prodded them to diagnos e their patients' headaches as symptoms of the very rare CD. (The use of Botox as a cosmetic wrinkle-remover wasn't at issue, but the typical injected dose for beauty treatment is tiny compared with that for a headache.)

Federal regulators were upset with Allergan because Botox derives from botulinum, one of the most toxic substances known to man. The high therapeutic doses, FDA officials say, increase the potential for the toxin to cause dangerous muscle weakness or paralysis.

Allergan's tactics worked fabulously. Between 1999 and 2006, the government says, Botox's headache sales grew by 1,407%. By 2007, total Botox sales exceeded $500 million. More than 70% of that was for unapproved uses.

This history didn't seem to enter into the FDA's review of Allergan's application to expand its marketing of the **Lap-Band**, a device surgically implanted around the stomach to suppress appetite. Up to now, the approved use has been for morbidly obese people who had failed to reduce with diet and exercise.

If you're 5 feet, 8 inches tall, you'd be eligible for the **Lap-Band** if you weighed 262, more than 100 pounds overweight, or 230 if you have an obesity-related condition such as diabetes. Under the newly approved standard, the latter figure drops to 197.

An FDA advisory panel, which gave preliminary approval to Allergan's application in December, wasn't entirely happy with the company's data supporting its safety and efficacy claims for the **Lap-Band** -- its own 149-patient study and six other studies, at least three of which were conducted by researchers with financial links to Allergan.

"I chastised Allergan for the cherry-picking they had done in the data," says John Kral, a member of the panel and a surgery professor at the State University of New York. The panel felt that a study of 149 patients wasn't good enough to establish the device's safety and efficacy over the long haul. Kral says he and the rest of the panel majority favored approval of Allergan's application even so, because they felt that the **Lap-Band**'s benefits outweighed the risks.

Others, such as Diana Zuckerman, head of the National Research Center for Women and Families and a longtime critic of the FDA, noticed that the panel seemed to give short shrift to numerous studies showing that weight loss results decline and side-effects increase with gastric bands over time. Zuckerman also points out that Allergan's study specifically excluded patients with a family history of autoimmune disease, even though that's a high-risk population for silicone implants like its **Lap-Band**.

In granting Allergan final approval for wider marketing of the **Lap-Band**, the FDA followed the advisory panel's recommendation that the company develop more long-term data -- but allowed it to step up the marketing of the **Lap-Band** now. What if the data show that the device becomes dangerous over time? By then hundreds of thousands, if not millions, more patients will be affected. "The time to ask for better research is before you say yes," Zuckerman says.

Nor does the FDA action take into account the overheated marketing that already surrounds the **Lap-Band**, such as the 1-800-GET-THIN billboards promoting this surgery. (Just the other day, two published studies showed that more traditional weight-loss surgery was more effective and no riskier than the band.) Do you think the GET-THIN gang might exploit the FDA approval to push their service even harder? My Magic 8-ball answers: "Signs point to yes."

Two weeks after Allergan pleaded out its criminal case, the FDA had a big ceremony honoring the now 96-year-old Kelsey. FDA Commissioner Margaret Hamburg pledged "to continue your great work here at the FDA."

If only we could count on that.

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